

Phosphate Esters. Part 3.¹ Formation of Sesquiterpene Hydrocarbons from *cis,trans*- and *trans,trans*-Farnesyl Diphenyl Phosphates

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Decomposition of *cis,trans*- and *trans,trans*-farnesyl diphenyl phosphates gives mixtures of both acyclic and cyclic sesquiterpene hydrocarbons consisting of β -farnesene, *cis*- and *trans*- α -farnesenes, and *cis*- α - and *trans*- α -, β -, and γ -bisabolenes, together with small quantities of *trans*-nerolidol and bisabolol. The proportion of the cyclic hydrocarbons was greater from the *cis,trans*-farnesyl diphenyl phosphate. Solvolysis of geranyl chloride gives linalool and geraniol but no cyclic products. The mechanisms of these reactions are discussed.

THE decompositions of geranyl and neryl diphenyl phosphates in anhydrous ether have been used as model reactions for the biosynthesis of monoterpenes from geranyl and neryl pyrophosphates.¹ We now report an extension of this work to studies on *cis,trans*- and *trans,trans*-farnesyl diphenyl phosphates, (1) and (2). The farnesyl pyrophosphates are commonly implicated as the immediate precursors in the biosynthesis of sesquiterpenes.²⁻⁴ The use of fully esterified phosphates as

models is justified since in the biological system the formal negative charges on the pyrophosphate residues would undoubtedly be 'neutralised' by combination with metal ions such as magnesium.

Initial studies were carried out on a mixture of *cis,trans*- and *trans,trans*-farnesyl diphenyl phosphates prepared from a commercial sample of farnesol containing 36% of the *cis,trans*- and 64% of the *trans,trans*-isomer. Decomposition of the farnesyl diphenyl phos-

¹ Part 2, R. C. Haley, J. A. Miller, and H. C. S. Wood, *J. Chem. Soc. (C)*, 1969, 264.

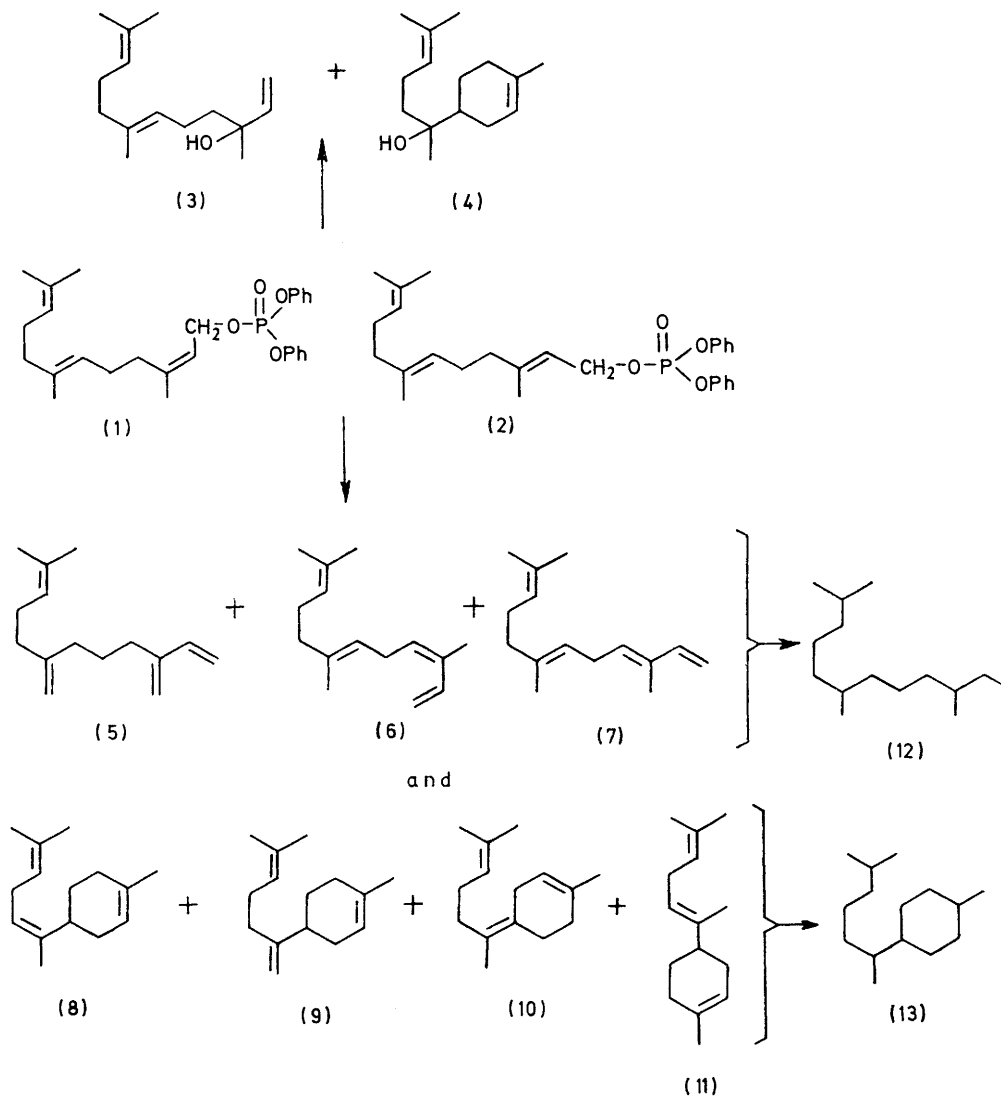
² G. Rücker, *Angew. Chem. Internat. Edn.*, 1973, **12**, 793.

³ J. B. Hendrikson, *Tetrahedron*, 1959, **7**, 82.

⁴ W. Parker, J. S. Roberts, and R. Ramage, *Quart. Rev.*, 1967, **21**, 331.

phates in diethyl ether gave a mixture of seven sesquiterpene hydrocarbons and two alcohols. The alcohols, which accounted for 5% of the mixture, were

The seven components were eventually identified as β -farnesene (5), *cis*- α -farnesene (6), *trans*- α -farnesene (7), *cis*- α -bisabolene (8), β -bisabolene (9), γ -bisabolene (10),

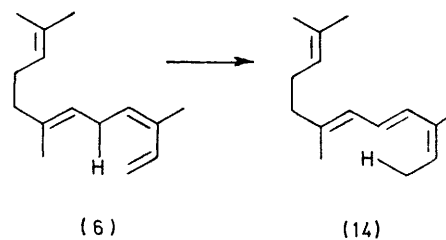


identified by their g.l.c. retention indices^{5,6} as *trans*-(\pm)-nerolidol (3) and bisabolol (4), present in the ratio 4:1. These alcohols probably resulted from hydrolysis of residual farnesyl diphenyl phosphates during work-up.

The hydrocarbon mixture was dehydrogenated over 10% palladised charcoal at 300–310 °C. Hydrogenation of the resultant mixture gave 2-methyl-6-*p*-tolylheptane. Hydrogenation of the original mixture of hydrocarbons gave a mixture of farnesane (12) and bisabolane (13). These results establish that the hydrocarbon products have structures based on the farnesane and bisabolane carbon skeletons.

The complex hydrocarbon mixture was separated by a combination of column chromatography on silica gel impregnated with silver nitrate and preparative g.l.c.

and *trans*- α -bisabolene (11). All but *cis*- α -farnesene were isolated in pure state and identified on the basis of



spectral data and g.l.c. retention indices. A pure sample of *cis*- α -farnesene was not obtained; at the higher temperatures employed for preparative g.l.c. this compound was no longer detected. The vapour from the g.l.c.

⁵ E. sz. Kovats, *Z. analyt. Chem.*, 1961, **181**, 351.

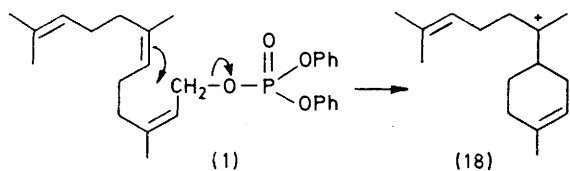
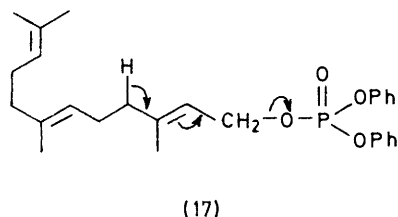
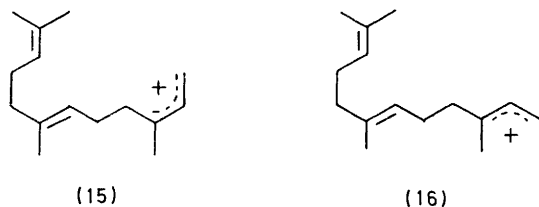
⁶ W. Rittersdorf and F. Cramer, *Tetrahedron*, 1968, **24**, 43.

column was condensed and found to contain traces of a conjugated triene (λ_{\max} , 271sh, 280, and 291sh nm). It has been reported that *cis*- β -ocimene undergoes a thermal

Hydrocarbons from the decomposition of farnesyl diphenyl phosphates

Hydrocarbon	Retention index ($I_{A_{170}}$)	% From <i>cis,trans</i> -isomer	% From <i>trans,trans</i> -isomer
β -Farnesene (5)	1 436	10.0	20.0
<i>cis</i> - α -Farnesene (6)	1 480	3.0	5.5
<i>trans</i> - α -Farnesene (7)	1 489	14.5	34.0
<i>cis</i> - α -Bisabolene (8)	1 513	ca. 9.0	ca. 5.0
β -Bisabolene (9)	1 525	39.0	20.5
γ -Bisabolene (10)	1 541	ca. 4.0	ca. 2.5
<i>trans</i> - α -Bisabolene (11)	1 555	22.5	12.5

1,5-sigmatropic rearrangement to give allo-ocimene whereas *trans*- β -ocimene does not rearrange.⁷ It is tentatively suggested that the second component is *cis*- α -farnesene, which rearranges at higher temperatures to allofarnesene (14). The sixth component was not fully characterized owing to lack of material. I.r. bands at 822 and 790 cm^{-1} suggest a bisabolene-type structure. This and the similarity of the i.r. spectrum to that of

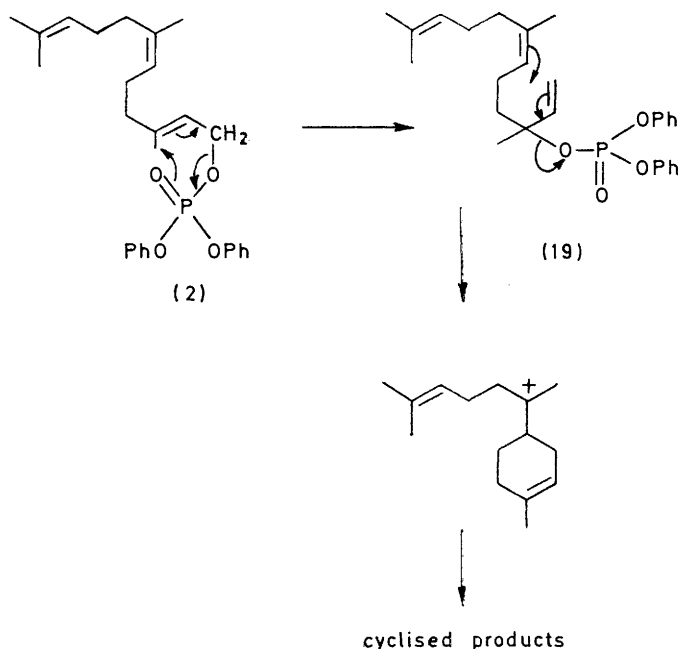


terpinolene enable this compound to be tentatively formulated as γ -bisabolene (10). The configurations of *cis*- and *trans*- α -bisabolene were assigned on the basis of their g.l.c. retention times. Hively⁸ has shown that for several trialkylethylenes the *cis*- has a shorter retention time than the *trans*-isomer.

Pure samples of *cis,trans*- and *trans,trans*-farnesol were obtained by preparative g.l.c. These were converted into their diphenyl phosphates, which were subsequently decomposed in ether. A mixture of the same seven sesquiterpene hydrocarbons was obtained

⁷ R. T. O'Connor and L. A. Goldblatt, *Analyt. Chem.*, 1954, **26**, 1726.

from both isomers, though in different proportions (see Table). The formation of the acyclic hydrocarbons from the farnesyl diphenyl phosphates could involve either ionization to give the carbocations (15) and (16) or a concerted mechanism [see (17)]. That *cis,trans*-farnesyl diphenylphosphate gave 75% of cyclic hydrocarbons on decomposition whereas *trans,trans*-farnesyl diphenyl phosphate gave only 40% is not surprising since the 6,7-double bond of the *cis,trans*-compound is well placed for an anchimerically assisted nucleophilic displacement of the diphenyl phosphate group [(1) \rightarrow (18)]. A similar explanation has been proposed to account for the higher proportion of cyclic products derived from neryl diphenyl phosphate than from the geranyl ester.^{1,6} The formation of cyclic compounds



from the *trans,trans*-compound demands further comment. There is considerable evidence for the configurational stability of allylic carbocations,⁹ and hence interconversion of (15) and (16) seems improbable. It seems likely that, as with the neryl system, an internal-return mechanism is operative [(2) \rightarrow (19)], analogous to that proposed for the formation of cyclic products from geranyl diphenyl phosphate. In support of this postulate we have now observed that no cyclic products are formed in the solvolysis of geranyl chloride (20), where an internal-return mechanism of this type cannot be envisaged, only linalool (23) and geraniol (24) being formed.

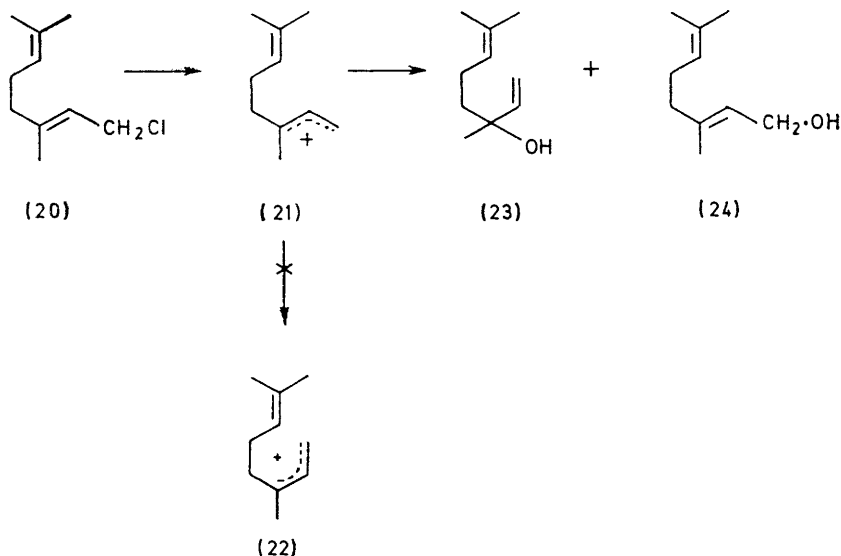
When the hydrocarbon mixture derived from farnesyl diphenyl phosphates was left in dry air for 3 days, a mixture of hydroperoxides was obtained which on treatment with potassium iodide in acetic acid gave α -curcumene (25), possibly as a result of autoxidation of γ -bisabolene.

⁸ R. A. Hively, *Analyt. Chem.*, 1963, **35**, 1921.

⁹ S. Winstein, *Bull. Soc. chim. France*, 1951, C43.

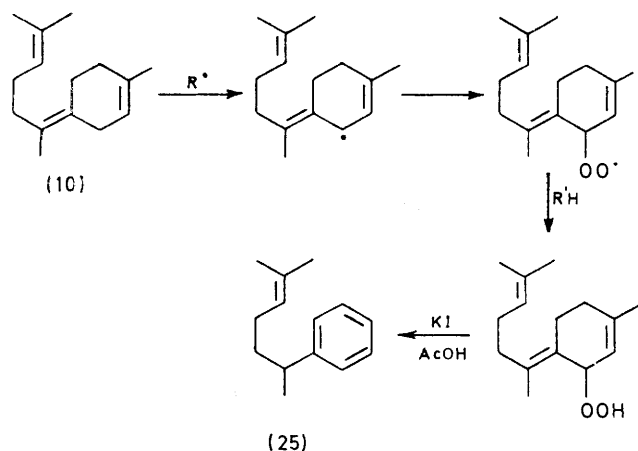
EXPERIMENTAL

I.r. spectra were obtained for liquid films or KCl discs on a Perkin-Elmer 257 spectrophotometer. N.m.r. spectra were run on a Perkin-Elmer R10 or R14 spectrometer (60 or 100 MHz) with tetramethylsilane as an internal standard. U.v. spectra were determined for ethanolic solutions with a Unicam SP 800A spectrometer. Mass spectra were run on an A.E.I. MS9 spectrometer. Analytical and preparative g.l.c. were carried out on a Pye 105 instrument with either column



X (20% Apiezon L on siliconised diatomite C) or column Y [10% Carbowax (PEG) 20M on siliconised diatomite C].

Farnesyl Diphenyl Phosphates.—These were prepared from commercial farnesol, consisting of the *cis,trans*- and *trans,trans*-isomers (36 and 64%, respectively) by treatment



with diphenyl phosphorochloridate in pyridine¹⁰ at 0 °C. The pure *cis,trans*- and *trans,trans*-isomers were prepared from the appropriate pure farnesols obtained from the commercial mixture by preparative g.l.c. on column Y at 170 °C.

Decomposition of Farnesyl Diphenyl Phosphates.—A solution of farnesyl diphenyl phosphate (25.3 g) in anhydrous

¹⁰ J. A. Miller and H. C. S. Wood, *J. Chem. Soc. (C)*, 1968, 1837.

ether (200 ml) was left at room temperature for 1 week, then extracted with dilute aqueous sodium hydrogen carbonate (100 ml), washed with water (100 ml), dried (Na_2SO_4), and evaporated. The residual oil (11.8 g) was chromatographed on neutral alumina (100 g) with light petroleum (b.p. 60–80 °C). The initial fractions (8.1 g) were shown by g.l.c. (column X at 170 °C) to consist of seven hydrocarbons, (A)–(G) of retention indices⁵ 1 436, 1 480, 1 489, 1 513, 1 525, 1 541, and 1 555.

The later fractions (0.4 g) consisted of two alcohols (column Y at 170 °C) of retention times 37.2 (alcohol 1) and 69.9 min (alcohol 2), in the ratio 4 : 1. Both were isolated as oils by preparative g.l.c. (column Y at 170 °C).

Alcohol 1. The i.r. spectrum showed ν_{max} (film) 3 380s, br, 3 085w, 994m, 920s, and 832m cm^{-1} , and was identical with that of authentic *trans*-(±)-nerolidol. The retention index on Apiezon L at 190 °C was 1 529 (lit.,⁶ I^A_{190} 1 530).

Alcohol 2. The i.r. spectrum showed ν_{max} (film) 3 430s, br, 3 050w, sh, 3 010w, 1 675m, 829w, and 798m cm^{-1} , τ (CCl_4) 4.62 (1 H, m), 4.87 (1 H, t, J 7 Hz), 6.40 (1 H, s, disappeared on deuteration), 7.70–8.20 (6 H, m), 8.30–8.40 (9 H, m), and 8.95 (3 H, d, J 2 Hz). The n.m.r. spectrum was identical with that published for bisabolol (4).¹¹ The retention index on Apiezon L at 190 °C was 1 706 (lit.,⁶ I^A_{190} 1 688).

Hydrogenation of the Hydrocarbon Mixture.—A sample of the mixture (1.0 g) was hydrogenated in methanol (25 ml) over 10% palladised charcoal (0.05 g). When uptake ceased (630 ml) the catalyst was filtered off and washed with light petroleum (b.p. 60–80°; 30 ml). Water (50 ml) was added to the combined filtrates. The petroleum layer was retained. The aqueous methanolic solution was further extracted with light petroleum (25 ml) and the combined extracts were dried (Na_2SO_4) and evaporated *in vacuo* leaving a sweet-smelling oil (0.72 g). G.l.c. (column X at 150 °C) showed that the oil consisted of two components, of retention times 34.5 (62%) and 56.4 min (38%). Both were isolated by preparative g.l.c. Component (i) had the same retention time (I^A_{150} 1 364) as authentic farnesane (12) (I^A_{150} 1 370);¹²

¹¹ C. D. Gutsche, J. R. Maycock, and C. T. Chang, *Tetrahedron*, 1968, **24**, 859.

¹² F. G. Fischer, *Annalen*, 1928, **464**, 69.

the i.r. spectra were also identical and the mass spectrum showed the molecular ion M^+ 212 ($C_{15}H_{32}$). The mass spectrum of the component (ii) (I_{150}^A 1 456) showed the molecular ion M^+ 210 ($C_{15}H_{30}$), and the i.r. spectrum showed ν_{\max} (film) 2 950s, 2 915vs, 2 865s, 1 455s, 1 446m, 1 379s, 1 369m, 1 340w, and 1 170m cm^{-1} , identical with that published¹³ for bisabolane (13).

Dehydrogenation of the Hydrocarbon Mixture.—A sample of the mixture (0.4 g) and 10% palladised charcoal (0.3 g) were heated under a current of nitrogen at 300–310 °C for 5 h. The mixture was cooled, ether (10 ml) was added, and the catalyst was filtered off and washed with ether (10 ml). The combined ethereal extracts were dried (Na_2SO_4) and evaporated *in vacuo* leaving an oil (0.24 g). The oil was hydrogenated in ethanol (25 ml) over 10% palladised charcoal (0.02 g). When uptake ceased (185 ml), the catalyst was filtered off and washed with light petroleum (b.p. 60–80 °C; 20 ml). Water (10 ml) was added to the combined filtrate and petroleum washings. The petroleum layer was retained, dried (Na_2SO_4), and evaporated *in vacuo* leaving a brown oil (0.21 g), which was chromatographed on silica gel (10 g). Elution with light petroleum (b.p. 60–80 °C) gave an oil (0.12 g). G.l.c. (column X at 150 °C) showed that the oil consisted of farnesane (25%) and 2-methyl-6-*p*-tolylheptane (70%). The latter was isolated by preparative g.l.c. on column X at 150 °C and had λ_{\max} 253 (log ϵ 2.16), 259.2 (2.34), 265 (2.43), 267.5 (2.42), and 273.5 nm (2.49); ν_{\max} (liq.) 3 095, 3 050, 3 022, 3 010, 1 895, 1 518, 817, and 722 cm^{-1} . The i.r. and u.v. data were identical with those published.¹⁴

Separation of Hydrocarbons.—The hydrocarbons obtained from the decomposition of farnesyl diphenyl phosphates were re-examined on a longer g.l.c. column (30 ft \times $\frac{3}{8}$ in 25% Apiezon L at 195 °C). From the relative retention times it was concluded that compound (B) was no longer present in detectable quantity. Preparative g.l.c. gave pure samples of compounds (A) and (C) but samples of compounds (E) and (G) contained some traces of a conjugated triene [λ_{\max} (hexane) 271sh, 280, and 291sh nm], although no conjugated triene was detected in the original hydrocarbon mixture.

The hydrocarbon mixture (3.5 g) was chromatographed on 10% silver nitrate–silica gel (70 g) with light petroleum (b.p. 60–80 °C) as eluant. The fractions were analysed by g.l.c. on column X at 170 °C. The first fraction contained compounds (D) and (G) only. The next consisted of compound (E) with traces of compounds (D), (F), and (G), and the final fraction consisted of compounds (A)–(C). Pure specimens of compounds (D)–(G) were obtained by preparative g.l.c. on the appropriate fraction. The compounds were readily oxidised in air and had to be kept under nitrogen.

Compound (A), β -farnesene (5), had retention index 1 436 on Apiezon L at 170 °C, λ_{\max} (hexane) 226 nm (log ϵ 4.225), ν_{\max} (film) 3 095w, 1 790w, 1 670w, 1 638w, 1 598s, 992s, 905sh, 895vs, and 835w cm^{-1} , τ (CCl_4) 3.65 (1 H, dd, J 18 and 12 Hz), 4.6–4.95 (4 H, m), 5.02br (2 H, s), 7.80 (4 H, m), 8.00 (4 H, m), 8.30 (3 H, s), and 8.38 (6 H, s), M^+ 204. The spectral data are identical with those published.¹⁵

Compound (C), *trans*- α -farnesene (7), had retention index 1 489 on Apiezon L at 170 °C; λ_{\max} (hexane) 233.5 nm

(log ϵ 4.40), ν_{\max} (film) 3 085w, 1 780w, 1 640m, 1 605m, 985m, 889s, and 825w cm^{-1} , τ (CCl_4) 3.70 (1 H, dd, J 18 and 10 Hz), 4.60 (1 H, t, J 7.5 Hz), 4.80–5.30 (4 H, m), 7.20 (2 H, t, J 7 Hz), 8.02 (4 H, m), 8.28 (3 H, s), and 8.40 (9 H, m). The spectral data are identical with those published for *trans*- α -farnesene.¹⁵ This compound was very unstable in air.

Compound (D), *cis*- α -bisabolene (8), had a retention index 1 513 on Apiezon L at 170 °C, ν_{\max} (film) 3 030w,sh, 3 000vw, 1 675vw, 1 650vw, 820m, and 795m cm^{-1} , τ (CCl_4) 4.60br (1 H), 4.92 (2 H, t, J 7.5 Hz), 7.33 (2 H, t, J 7.5 Hz), 7.60–8.20 (5 H, m), and 8.40 (14 H, m), M^+ 204.

Compound (E), β -bisabolene (9),¹³ had retention index 1 525 on Apiezon L at 170 °C; ν_{\max} (film) 3 080w, 3 010vw, 1 640m, 888s, 825w, and 795w cm^{-1} , τ (CCl_4) 4.60br (1 H, m), 4.90br (1 H, m), 5.26br (2 H, s), 7.60–8.15 (9 H, m), and 8.15–8.45 (11 H, m), M^+ 204.

Compound (F) had retention index 1 541 on Apiezon L at 170 °C, but because of lack of material few spectral data were available. However, on the basis of the i.r. spectrum, the compound was tentatively characterised as γ -bisabolene (10); ν_{\max} (film) 3 040w,sh, 3 010w,sh, 1 674vw, 822m, and 790w cm^{-1} .

Compound (G), *trans*- α -bisabolene (11), had retention index 1 555 on Apiezon L at 170 °C; ν_{\max} (film) 3 044w, 3 010w, 1 670vw, 1 659w, 829m, 799m, and 790w cm^{-1} , τ (CCl_4) 4.62br (1 H, m), 4.90br (2 H, m, J 7 Hz), 7.38 (2 H, t, J 7 Hz), 7.60–8.20 (5 H, m), and 8.40 (14 H, m), M^+ 204.

Atmospheric Oxidation of Hydrocarbons from the Decomposition of Farnesyl Diphenyl Phosphates.—A sample of the hydrocarbon mixture (0.5 g) was kept in dry air for 3 days, during which time the viscous oil was converted into a glassy mass, ν_{\max} 3 370vs,br cm^{-1} . Potassium iodide (3 g) in glacial acetic acid (50 ml) was added to the mixture, whereupon iodine was immediately liberated. The mixture was kept at 0 °C for 12 h and then the iodine was reduced with dilute aqueous sodium thiosulphate. The mixture was extracted with methylene chloride (2 \times 25 ml) and the extracts were washed with dilute aqueous sodium hydrogen carbonate (2 \times 25 ml) and with water (25 ml). The methylene chloride solution was dried (Na_2SO_4) and evaporated leaving a yellow viscous oil (0.22 g).

G.l.c. analysis on column X at 170 °C showed that sesquiterpene hydrocarbons accounted for <20% of the mixture. Four hydrocarbons of retention times 17.6, 23.7, 26.9, and 31.2 min were present. The compound of retention time 26.9 min (*ca.* 40% of the hydrocarbons) was isolated by preparative g.l.c. (10 mg). The i.r. spectrum showed ν_{\max} (film) 3 080w, 3 040w, 3 008w, 1 891w, 1 684w, 1 514s, 830sh, 812vs, and 720m cm^{-1} , and was identical with that published for α -curcumene (25).⁴

Hydrolysis of Geranyl Chloride.—A mixture of geranyl chloride¹⁶ (8.6 g, 0.05 mol) and 0.2M-sodium hydroxide (500 ml) was stirred at room temperature for 24 h, then extracted with ether (3 \times 50 ml). The combined extracts were washed with water (2 \times 50 ml), dried (Na_2SO_4), and evaporated leaving a yellow oil (4.2 g). G.l.c. analysis on column Y at 150 °C showed that the oil consisted of linalool (73%), I_{150}^P 1 546 (lit.,¹⁷ 1 545), and geraniol (25%), I_{150}^P 1 856 (lit.,¹⁷ 1 845).

[6/1068 Received, 4th June, 1976]

¹³ J. Pliva, V. Herout, and F. Sorm, *Coll. Czech. Chem. Comm.*, 1951, **16**, 158.

¹⁴ V. K. Honwad and A. S. Rao, *Tetrahedron*, 1965, **21**, 2593.

¹⁵ K. E. Murray, *Austral. J. Chem.*, 1969, **22**, 197.

¹⁶ G. Stork, P. A. Grieco, and M. Gregson, *Tetrahedron Letters*, 1969, 1393.

¹⁷ F. Cramer and W. Rittersdorf, *Tetrahedron*, 1967, **23**, 3015.